

ORIGINAL ARTICLE

# Effect of gluten-free diet and compliance on quality of life in pediatric celiac disease patients

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## Key words

pediatric symptom checklist, psychosocial, compliance barrier, well-being.

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## Abstract

**Background:** Quality of life (QOL) in children with celiac disease (CD) has been sparsely studied.

**Aims:** We aimed to study QOL in pediatric CD and the effect of a gluten-free diet (GFD) in a North Indian population.

**Methods:** QOL was assessed at baseline and 6 months after GFD using a pediatric symptom checklist (PSC) score. The effect of GFD was assessed using a CD-specific questionnaire on domains such as dietary compliance, parental behavior and perceptions, children's feeling, and difficulty identifying gluten-free foods.

**Results:** A total of 60 CD children (age  $6.03 \pm 0.42$  years, range: 2–12 years, M:F 2:1) were prospectively enrolled. The median PSC score at baseline was 11.5 (2–35), which showed a statistically significant improvement after GFD to 2.5 (0–34) ( $P < 0.001$ ). Significant concerns regarding specific domains emerged: difficulty in maintaining GFD 26.2%, at school 14.3%, at parties 43.2%, poor taste 11.4%, special diet a burden 28.5%, felt left out at school or friend's home 40.9%, felt different from other kids 40.9%, felt embarrassed to bring GFD to parties 54.6%, felt angry about following a special diet 56.8%, felt not invited out for meals because of CD 13.6%, and difficulty determining if food available was gluten free in 75%.

**Conclusion:** GFD has a significant impact on emotional, behavioral, and psychosocial domains in children with CD. Proper labeling of commercially available food items, counseling, and patient support groups are the need of the hour.

## Introduction

Celiac disease (CD) is a common autoimmune disorder caused by the ingestion of gluten. Gluten triggers an autoimmune phenomenon in a genetically susceptible individual, resulting in the infiltration of the lamina propria with chronic inflammatory cells, resulting in progressive shortening in small intestinal villus height.<sup>1</sup> CD is increasingly being reported in various Southeast Asian and Middle Eastern countries such as India, Pakistan, Iran, etc.<sup>2–4</sup>

A diagnosis of CD entails strict lifelong adherence to a gluten-free diet (GFD). A diagnosis of CD and commitment to GFD affect various domains of a child's growth and development, such as physical growth, self-concept, and identity. Disease realization adversely affects his or her health-related quality of life (HRQoL).<sup>5,6</sup> Not only the affected children, but also their parents and relatives need immense professional support, education, and guidance regarding the children's disease and management.<sup>6,7</sup> Strict adherence to GFD is also perceived as a burden due to high cost, dietary restriction, social activity restriction, and health worries.<sup>8</sup>

Quality-of-life assessment can be carried out using both generic and disease-specific questionnaires.<sup>9–11</sup> Generic questionnaires can be used for the comparison of quality of life (QoL) between two unrelated diseases. Disease-specific questionnaires address the issues specific to a particular disease and thus yield better information pertaining to a particular disease. Pediatric symptom checklist is a generic questionnaire that has been developed and validated in a large cohort to assess a child's psychosocial parameters.<sup>12</sup> CD-specific questionnaires that have been used in various studies have assessed a child's feelings, parental behavior and perceptions, effect of CD on child's travel, eating out, and factors affecting compliance with GFD.<sup>13–15</sup> Few studies have utilized PSC (a generic questionnaire) and a customized disease-specific questionnaire to assess QoL in pediatric CD patients.<sup>14,16</sup> A study from Italy studied the impact of GFD on psychosocial parameters (using PSC) and neurological parameters (using a specific questionnaire).<sup>17</sup>

Studies on the pediatric population regarding QoL in CD are limited.<sup>6,13–18</sup> Moreover, in most studies, compliance with GFD is assessed retrospectively.<sup>14,16</sup> In fact, even the history of recall was confined to just 5 days in the study by Garg *et al.* A

study from Sweden was retrospective in design, and it did not include patients younger than 8 years of age.<sup>6</sup> The only study that evaluated the effect of GFD prospectively on neurological and psychosocial parameters (by use of PSC) did not include disease-specific questionnaires to demonstrate improvement in other domains such as eating, travel, factors affecting compliance, etc.<sup>17</sup> Use of variable scoring systems by different studies to compare QoL with respect to different domains has made the existing studies difficult to compare.

Some studies showed improvement in quality-of-life parameters after GFD implementation, whereas others failed to show a benefit.<sup>5</sup> However, there is no study that has prospectively assessed the effect of CD and GFD on psychosocial and other disease-specific domains in the pediatric population.

The aims of our study were to evaluate the impact of CD on psychosocial parameters in children using the PSC.<sup>12</sup> We also aimed to assess the effect of GFD on psychosocial parameters and QoL using disease-specific questionnaires.

## Methodology

This prospective follow-up study was carried out at a tertiary care center in North India from June 2014 to November 2015. Written informed consent was obtained from all parents before enrolling in the study. Institutional ethical clearance was obtained prior to commencement of the study. Sixty pediatric patients were prospectively enrolled. Children between 2 and 12 years of age with symptoms suggestive of CD and elevated tissue transglutaminase were included. CD was diagnosed on the basis of standard European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) criteria.<sup>19</sup> Patients with chronic illnesses (chronic kidney disease, cirrhosis, and congestive cardiac failure) and parents who denied consent for endoscopy in their child were excluded from the study.

For all patients, a detailed history was taken and physical examination conducted at baseline. An esophagogastroduodenoscopy was performed using an Olympus GIF 180 H endoscope (Olympus medical systems corp 2951 Ishikawa-cho, Hachiojishi, Tokyo, Japan) with a CV 180 processor, and duodenal biopsies were taken at baseline from all patients. Complete blood counts and biochemical investigations were performed in all patients at baseline only. The serum IgA tTG antibody was carried out for all enrolled patients using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Thermo Scientific, Freiburg, Germany) using recombinant human tTG, with a 10 EliA U/mL cut-off point for the positive test (range 0.1 to >128) at baseline.

Both the generic (PSC) and disease-specific questionnaires were used to assess the QoL in children with CD. Baseline assessment of a child's psychosocial parameters was performed with the help of the PSC questionnaire.<sup>12</sup> Each PSC item was rated never: 0, sometimes: 1, and often: 2. The total score was calculated and recorded as a dichotomous variable. PSC scores of 28 or higher for children aged >6 years and 24 or higher for children between 2 and 6 years of age were considered to be emotional and psychosocial impairment.<sup>12</sup> The questionnaires were made in Hindi/Punjabi/English (local languages used) for ease of understanding. In the child, evaluation was performed in

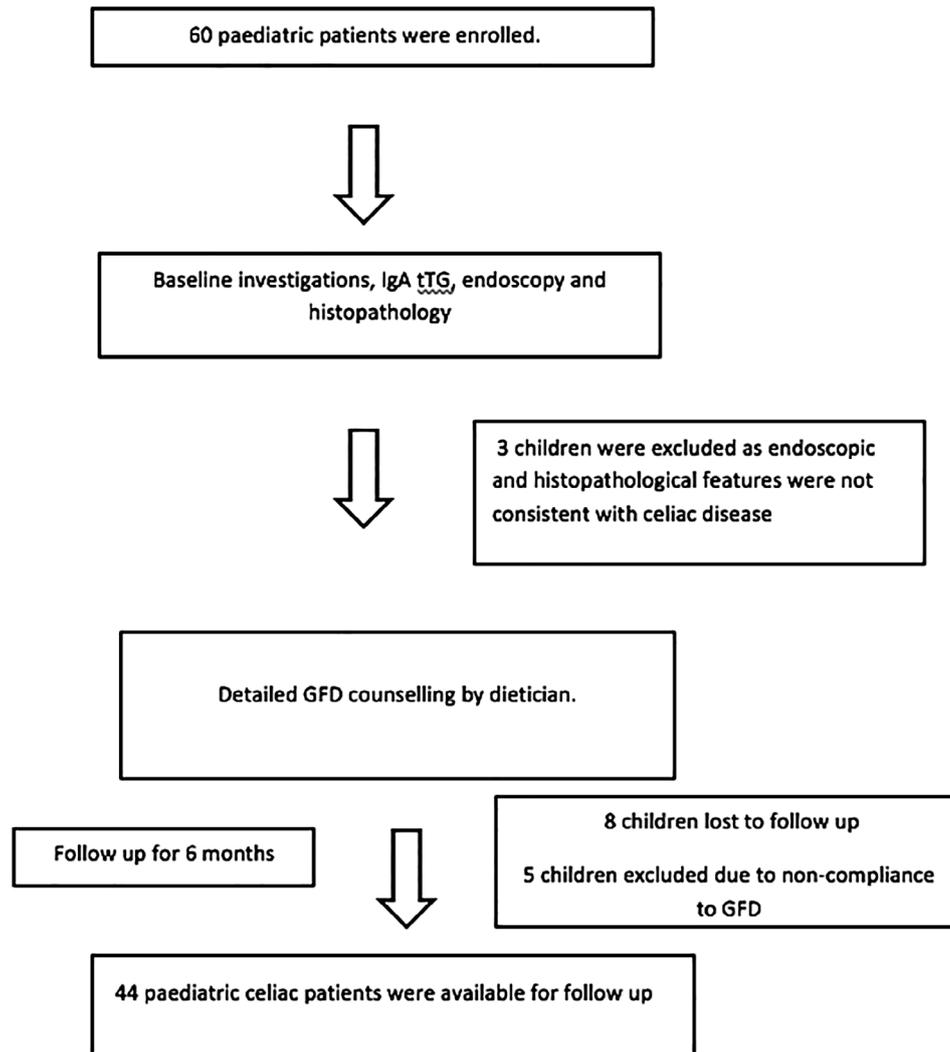
the presence of the mother, and clarification with mother was carried out whenever necessary.

After initial evaluation, the need of adherence to GFD was addressed, and detailed counseling regarding the need to adhere to strict GFD, nutritional requirements, and available local gluten-free preparations was carried out by an expert dietician. Follow up of children and their parents was initially conducted every month for 3 months and then after 6 months of GFD. Those patients who were compliant with GFD were evaluated after 6 months of GFD. A follow-up history of symptoms was taken, and weight and height were measured after 6 months of GFD. A follow-up assessment of psychosocial parameters was conducted (using PSC questionnaire) after 6 months of being on GFD.

Previous studies have used CD-specific questionnaires, which included questions on demographic profile, history of illness, parents' behavior, knowledge and understanding of disease, barriers to compliance and the effect of CD on feelings of children, eating out, and travel.<sup>13,14,16</sup> The questionnaire used in our study was adapted from a study by Chauhan *et al.*, which has been validated in India.<sup>14</sup> We included questions on barriers to dietary compliance and parental behavior and perceptions.<sup>14</sup> The effect of CD and GFD on the feelings of children with respect to friends, school, or teachers; feelings about following special GFD; and difficulty in determining if food available at various places like schools/supermarkets/restaurants was gluten free were also included in our questionnaire.<sup>14</sup> The feelings of the child and the difficulty faced by him or her to determine whether food available was free from gluten was expressed as all the time, most of the time, sometimes, or never, and children falling in each category were expressed numerically and by percentages. These disease-specific questionnaires were administered by the investigator after the children were on GFD for 6 months.

The effect of CD and GFD on issues affecting a child's compliance with GFD and parental behavior and parental perceptions were assessed by asking questions about diet maintenance at school, diet maintenance at party/marriage, taste of GFD, diet being a special burden, discussion of the child's disease with society, and parental beliefs of likely problems the child might face during marriage. Effects of CD and GFD on the feelings of children with respect to friends, school, or teachers; feelings about following special GFD, and difficulty in determining if food available was gluten free were assessed by enquiring about feeling left out at school/friend's home, feeling different from other kids, feeling embarrassed to bring GFD to parties, feeling angry about following a special diet, feeling their teachers and friends did not understand the disease, feeling they could be healthy without following a special diet, finding it difficult to determine if food was gluten free from labels, and feeling that they were not invited for meals because of CD.

**Statistical analysis.** All data was acquired prospectively in the enclosed proforma and was finally entered into the computer using SPSS/Microsoft Excel format for analysis. The data were analyzed using SPSS software. Symptoms were presented as numbers and percentages. The McNemar test was applied to see the difference between pre- and post-GFD data. QoL was presented as median and interquartile range, and this was compared using the Wilcoxon Signed Rank test. All calculations were



**Figure 1** Study protocol.

performed using SPSS version 17 (Statistical Packages for the Social Sciences, Chicago, IL, USA).  $P$  value  $\leq 0.05$  was considered significant.

## Results

In our study, 60 patients were enrolled; however, 3 patients were excluded as endoscopic and histological features were not consistent with CD (Fig. 1). Thirteen patients were excluded because of loss to follow up (8 patients) or noncompliance with GFD (5 patients), and 44 pediatric patients were followed up for 6 months. The mean age of the study group was  $6.03 \pm 0.42$  years, with 68.2% ( $n = 30$ ) patients being males. Median PSC scores before starting GFD were 11.5 (2–35). PSC score showed significant decline after 6 months of GFD. Median PSC scores improved from 11.5 (2–35) to 2.5 (0–34) after 6 months of GFD ( $P < 0.001$ ). Abnormal PSC scores were noted in five (11.4%) patients before starting GFD, whereas only one (2.3%) patient had abnormal scores after 6 months of GFD.

**Table 1** Clinical features of patients before and after 6 months of the gluten-free diet

Symptoms	Pre-GFD ( $n$ [%])	Post-GFD ( $n$ [%])
Diarrhea	23 (52.3%)	1 (2.3%)
Failure to thrive	30 (68.2%)	2 (4.5%)
Pallor/anemia	26 (59.1%)	2 (4.5%)
Abdominal distention	24 (54.5%)	2 (4.5%)
Oral ulcers	5 (11.4%)	1 (2.3%)
Weight loss	26 (59.1%)	0
Constipation	10 (22.7%)	0
Fatigue	24 (54.5%)	1 (2.3%)
Skin rash	3 (6.8%)	0
Vomiting	8 (18.2%)	0
Height (mean), SD	108.66 cm, 16.96 cm	112.30 cm, 16.71 cm
Weight (mean), SD	18.09 kg, 7.63 kg	20.10 kg, 8.03 kg

GFD, Gluten-free diet.

**Table 2** Difficulties in child's compliance with GFD and parental behavior and perceptions

Parameter	Response	Number (%)
Finds keeping diet (responded patients—42 [95.5%])	Difficult	4 (9.5%)
	Fairly difficult	7 (16.7%)
	Easy	31 (73.8%)
Diet maintenance difficult at school (responded patients—42 [95.5%])	Not applicable	7 (16.7%)
	Yes	6 (14.3%)
	No	29 (69%)
Diet maintenance difficult at family party/marriage (responded patients—44 [100%])	Not applicable	2 (4.5%)
	Yes	19 (43.2%)
	No	23 (52.3%)
Finds taste of GFD (responded patients—44 [100%])	Very good	3 (6.8%)
	Good	27 (61.4%)
	Satisfactory	9 (20.5%)
	Bad	5 (11.4%)
Special diet is burden for you (responded patients—42 [95.5%])	Frequently	3 (7.1%)
	Fairly	9 (21.4%)
	Hardly	30 (71.4%)
Discuss the child's condition with (responded parents—42 [95.5%])	Everybody	10 (23.8%)
	Family once	32 (76.2%)
	Do not discuss	0
Does the child have problem with marriage (responded parents—42 [95.5%])	Yes	36 (85.7%)
	No	6 (14.3%)

GFD, gluten-free diet.

There was an improvement in median weight and height after 6 months of GFD. There was improvement in a majority of clinical parameters after 6 months of GFD as shown in Table 1.

Effects of CD and GFD on issues affecting a child's compliance with GFD and parental behavior and parental perceptions were affected as depicted in Table 2. Feelings of children with respect to friends, school, or teachers about following special GFD were affected as shown in Table 3.

## Discussion

In this study, we have evaluated the QoL of children with CD using PSC to assess psychosocial parameters in 44 patients who were compliant with GFD. On follow up at 6 months, there was an improvement in symptoms of CD, such as weight, height, failure to thrive, anemia, diarrhea, etc. PSC scores improved from 11.5 to 2.5 after starting GFD. There were several barriers to dietary compliance, such as maintaining the diet at school, party/marriages; finding the taste of GFD unsatisfactory; and special diet being a burden. The effect of CD and GFD on feelings of children with respect to friends, school, or teachers and feelings about following special GFD was significantly affected. There was significant difficulty in determining if food available at various places like schools/supermarkets/restaurants was free from gluten.

Various scoring systems exist to assess the QoL in the pediatric population, such as the Ontario Child Health Study (OCHS),<sup>20</sup> Nordic Quality of Life Questionnaire for Children,<sup>21</sup> TACQOL,<sup>22</sup> Paediatric quality of life inventory 4.0<sup>23</sup> etc., each of which assesses various domains in a child's functioning. It is important for a scoring system to address vital domains for a child's well-being, such as social, psychosocial, emotional, behavioral, physical, etc. PSC is a one-page questionnaire filled up by a parent, reflecting his or her assessment of the child's psychosocial functioning.<sup>12</sup> However, it is known that parental assessment of child's condition may overestimate the child's actual QoL.<sup>24,25</sup> Moreover, compliance issues, parental behavior and perceptions, child's feeling, eating out, and travel are important issues that need special attention in the context of pediatric CD. Disease-specific questionnaires have been shown to improve the assessment of QoL compared to generic questionnaires in the past.<sup>26</sup>

In the current study, median values of PSC were 11.5 at baseline, which reduced to 2.5 after 6 months of GFD ( $P < 0.001$ ). The number of patients with abnormal PSC scores also reduced from 5 (11.4%) to 1 (2.3%) after 6 months of GFD. So, GFD improved scores, thereby implying that GFD significantly improved QoL. In another study on the comparison of CD children who were compliant with GFD with those who were noncompliant, higher PSC scores were noted in children who were noncompliant with GFD (16.1 vs. 20.3).<sup>14</sup> In a study by

**Table 3** Effect of maintaining a special diet, eating out, and travel

Parameter	All the time	Most of time	Some of time	Never	Not answered
Feel left out activities at school or friends home ( <i>n</i> [%])	1 (2.3%)	3 (6.8%)	14 (31.8%)	25 (56.8%)	1 (2.3%)
Felt different from other kids ( <i>n</i> [%])	2 (4.5%)	5 (11.4%)	11 (25%)	25 (56.8%)	1 (2.3%)
Felt embarrassed to bring Gluten free diet to parties ( <i>n</i> [%])	3 (6.8%)	3 (6.8%)	18 (41%)	17 (38.6%)	3 (6.8%)
Felt angry about following a special diet ( <i>n</i> [%])	2 (4.5%)	7 (16%)	16 (36.3%)	19 (43.2%)	0
Felt their teacher and friends did not understand the disease ( <i>n</i> [%])	1 (2.3%)	1 (2.3%)	4 (9%)	33 (75%)	5 (11.4%)
Felt that they can be healthy without following a special diet ( <i>n</i> [%])	2 (4.5%)	6 (13.6%)	8 (18.2%)	28 (63.6%)	0
Found it difficult to determine if food was gluten free from labels ( <i>n</i> [%])	32 (72.7%)	0	1 (2.3%)	11 (25%)	0
Felt that they were not invited out for meals because of celiac disease ( <i>n</i> [%])	0	4 (9.1%)	2 (4.5%)	37 (84.1%)	1 (2.3%)

Garg *et al.*, it was also shown that mean PSC score for the GFD-compliant group was 8.3 compared to 14.6 in the noncompliant group. A study from Italy compared children (aged 4–16 years) with newly diagnosed CD (40 patients), CD in remission after GFD (54 patients), and potential CD (45 patients) for neurological and psychosocial problems using PSC.<sup>17</sup> Mean PSC scores were higher in the newly diagnosed CD group (14.81) compared to the CD in remission (12.27) group.<sup>17</sup> Moreover, mean PSC scores in the newly diagnosed CD group were 14.81, which improved significantly to 10.32 after 1 year of GFD. It has been shown in past that, with increasing age of CD children/adolescents, mean PSC scores increase.<sup>16</sup> Increase in psychosocial problems with increasing age is likely due to increased peer pressure, travel, and more exposure to a variety of foods. As we included patients who were younger (2–12 years), lower PSC scores are expected.

Children with CD experienced difficulties regarding adherence to GFD. Approximately one third of patients found the taste of GFD satisfactory or bad. Disliking the taste of GFD can be a major factor impeding strict compliance with GFD, especially in pediatric age group.<sup>16</sup> A study by Garg *et al.* found that around 25% children found the taste of GFD satisfactory or bad, which could result in noncompliance with GFD.<sup>16</sup> Of the parents in our study, 76% had constant concern about their child's health, and they used to discuss the condition of the child with the family at least once. Parents' knowledge about the disease, its likely complications, and the benefits of adhering to strict GFD and their attitude has demonstrated better compliance with GFD in the past.<sup>14,16,27</sup> It is extremely important for parents and close relatives to discuss the disease with their child to allay his or her fears and anxiety regarding CD. Sociocultural beliefs in North India are a major reason for marriage-related anxiety amongst a vast majority of parents in our study population.

CD and GFD affected the feelings of children with respect to friends, school, or teachers. Children also felt embarrassed and angry about having to follow a special diet. In a study by Chauhan *et al.*, 25.4% children compliant with GFD felt left out of activities at school or friends' home at least sometimes, whereas 33% patients resented following a special diet.<sup>14</sup> In a study by Garg *et al.*, around 52% children felt angry about following a special diet at least sometimes, whereas 9% children felt they were not invited out most of the time in the compliant group. However, feelings of being left out and resentment to compulsory GFD were much higher in the noncompliant group in both the above-mentioned studies.<sup>14,16</sup> In a Canadian study analyzing QoL in CD children younger than 16 years of age, 23% patients felt angry all or most of the time about following strict GFD, whereas more than 50% felt different from other kids because of their disease at least sometimes.<sup>13</sup> In a study by Rashid *et al.*, around 53% patients felt that their teachers and friends did not understand them at least sometimes. Parental and social support and knowledge about disease forms an integral part of the holistic management of CD patients.<sup>27</sup>

A majority of children in our study found it difficult to determine if available food was gluten free all of the time. Non-availability of GFD and absence of labeling on available food are common problems faced by children and adolescents suffering from CD.<sup>13,18,27</sup>

This is the first study that has evaluated the impact of CD and GFD on pediatric quality-of-life parameters assessed by PSC and disease-specific questionnaires by following up patients prospectively. We included PSC (a questionnaire assessing the psychosocial parameters, which is filled by the parent) and disease-specific questionnaires (which were filled by interviewer), hence providing a more neutral view of a child's QoL.

Our study has certain limitations. First, our CD group did not have a control group to compare various quality-of-life parameters. We only included patients with CD who were compliant with GFD for 6 months in our final analysis. Comparison of groups compliant and noncompliant with GFD could have yielded differences amongst various domains assessing QoL. In our study, the assessment of the effect of GFD was carried out only for 6 months. The PSC questionnaire used in our study to assess QoL was filled by the parent regarding his or her child. This may be an inherent limitation to correctly gauge the child's emotional and psychological well-being. The PSC questionnaire we used is validated for the age group of 4–15 years; however, we included patients from 2 to 12 years of age in our study.<sup>12</sup> We did not perform a repeat IgA/ttg serology testing or esophago-gastroduodenoscopy with duodenal biopsies after 6 months of compliance with GFD.

In Western countries, with increasing awareness about CD and its complications and stringent policy decisions, proper labeling of commercially available food for the presence of gluten has started.<sup>28</sup> In fact, there are separate counters for gluten-free food at restaurants, and the amount of gluten in certain food products is even specified. However, in Asia and the Indian subcontinent, proper labeling of available food products is not performed. Although the Indian Council of Medical Research (ICMR) has advocated detailed counseling of parents and children regarding the need for life-long compliance with GFD by physicians and trained dieticians, it is practically not carried out in a majority of centers across Southeast Asia and the Middle East. There is a need to increase awareness and bring about strict policy decisions regarding proper labeling of food.

To conclude, our study has shown a significant reduction in PSC scores in children with CD after being compliant with GFD. It has further highlighted the impact of GFD on emotional, behavioral, and psychosocial domains in children. Policy decisions ensuring proper labeling of food items available commercially, more availability of gluten-free food items in supermarkets/restaurants and school canteens, proper counseling of CD affected children by trained dieticians, and patient support groups is the need of the hour to improve the QoL of children with CD.

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